1/14 SEQUENCE LISTING <110> HANSA MEDICAL RESEARCH AB <120> METHOD AND TREATMENT <130> N.87400B SER/SJB <160> 10 <170> PatentIn version 3.1 <210> 1 <211> 484 <212> PRT <213> Streptococcus pyogenes <400> 1 5 10 25 40 55 75 85 90

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 Ala Lys Leu Arg Ala Gly Lys Ala Ser Asp Ser Gln Thr Pro Asp Thr
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 Gln Leu Pro Ser Thr Gly Glu Thr Ala Asn Pro Phe Phe Thr Ala Ala
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Asp Ser Asp Trp Pro Phe Cys Ser Asp Glu Asp Trp Asn Tyr Lys Cys 20 Pro Ser Gly Cys Arg Met Lys Gly Leu Ile Asp Glu Val Asn Gln Asp 35 40 Phe Thr Asn Arg Ile Asn Lys Leu Lys Asn Ser Leu Phe Glu Tyr Gln 50 Lys Asn Asn Lys Asp Ser His Ser Leu Thr Thr Asn Ile Met Glu Ile 70 Leu Arg Gly Asp Phe Ser Ser Ala Asn Asn Arg Asp Asn Thr Tyr Asn 85 Arg Val Ser Glu Asp Leu Arg Ser Arg Ile Glu Val Leu Lys Arg Lys 100 Val Ile Glu Lys Val Gln His Ile Gln Leu Leu Gln Lys Asn Val Arg 115 120 Ala Gln Leu Val Asp Met Lys Arg Leu Glu Val Asp Ile Asp Ile Lys 130 135 Ile Arg Ser Cys Arg Gly Ser Cys Ser Arg Ala Leu Ala Arg Glu Val 150 Asp Leu Lys Asp Tyr Glu Asp Gln Gln Lys Gln Leu Glu Gln Val Ile 165 170 Ala Lys Asp Leu Leu Pro Ser Arg Asp Arg Gln His Leu Pro Leu Ile 180 185 Lys Met Lys Pro Val Pro Asp Leu Val Pro Gly Asn Phe Lys Ser Gln 195 200 Leu Gln Lys Val Pro Pro Glu Trp Lys Ala Leu Thr Asp Met Pro Gln 210 215 Met Arg Met Glu Leu Glu Arg Pro Gly Gly Asn Glu Ile Thr Arg Gly 225 230 235 Gly Ser Thr Ser Tyr Gly Thr Gly Ser Glu Thr Glu Ser Pro Arg Asn 245 Pro Ser Ser Ala Gly Ser Trp Asn Ser Gly Ser Ser Gly Pro Gly Ser 260 265 Thr Gly Asn Arg Asn Pro Gly Ser Ser Gly Thr Gly Gly Thr Ala Thr 275 280

Trp Lys Pro Gly Ser Ser Gly Pro Gly Ser Thr Gly Ser Trp Asn Ser 290 295 Gly Ser Ser Gly Thr Gly Ser Thr Gly Asn Gln Asn Pro Gly Ser Pro 310 Arg Pro Gly Ser Thr Gly Thr Trp Asn Pro Gly Ser Ser Glu Arg Gly 325 Ser Ala Gly His Trp Thr Ser Glu Ser Ser Val Ser Gly Ser Thr Gly 340 Gln Trp His Ser Glu Ser Gly Ser Phe Arg Pro Asp Ser Pro Gly Ser 355 360 Gly Asn Ala Arg Pro Asn Asn Pro Asp Trp Gly Thr Phe Glu Glu Val 370 375 Ser Gly Asn Val Ser Pro Gly Thr Arg Arg Glu Tyr His Thr Glu Lys 390 385 Leu Val Thr Ser Lys Gly Asp Lys Glu Leu Arg Thr Gly Lys Glu Lys 405 410 Val Thr Ser Gly Ser Thr Thr Thr Arg Arg Ser Cys Ser Lys Thr 420 425 Val Thr Lys Thr Val Ile Gly Pro Asp Gly His Lys Glu Val Thr Lys 435 440 Glu Val Val Thr Ser Glu Asp Gly Ser Asp Cys Pro Glu Ala Met Asp 455 Leu Gly Thr Leu Ser Gly Ile Gly Thr Leu Asp Gly Phe Arg His Arg 465 470 475 His Pro Asp Glu Ala Ala Phe Phe Asp Thr Ala Ser Thr Gly Lys Thr 485 Phe Pro Gly Phe Phe Ser Pro Met Leu Gly Glu Phe Val Ser Glu Thr 500 505 Glu Ser Arg Gly Ser Glu Ser Gly Ile Phe Thr Asn Thr Lys Glu Ser 515 520 Ser Ser His His Pro Gly Ile Ala Glu Phe Pro Ser Arg Gly Lys Ser 530 535 Ser Ser Tyr Ser Lys Gln Phe Thr Ser Ser Thr Ser Tyr Asn Arg Gly 545 550 Asp Ser Thr Phe Glu Ser Lys Ser Tyr Lys Met Ala Asp Glu Ala Gly 560 565 Ser Glu Ala Asp His Glu Gly Thr His Ser Thr Lys Arg Gly His Ala 575 580 585 Lys Ser Arg Pro Val Arg Gly Ile His Thr Ser Pro Leu Gly Lys Pro 590 595 600 Ser Leu Ser Pro <210> 6

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Cys Gly Ile Ala Asp Phe Leu Ser Thr Tyr Gln Thr Lys Val Asp Lys
                                           35
Asp Leu Gln Ser Leu Glu Asp Ile Leu His Gln Val Glu Asn Lys Thr
                      45 .·
Ser Glu Val Lys Gln Leu Ile Lys Ala Ile Gln Leu Thr Tyr Asn Pro
                                     65
Asp Glu Ser Ser Lys Pro Asn Met Ile Asp Ala Ala Thr Leu Lys Ser
              75
Arg Ile Met Leu Glu Glu Ile Met Lys Tyr Glu Ala Ser Ile Leu Thr
                              95
                                                 100
His Asp Ser Ser Ile Arg Tyr Leu Gln Glu Ile Tyr Asn Ser Asn Asn
                          110
Gln Lys Ile Val Asn Leu Lys Glu Lys Val Ala Gln Leu Glu Ala Gln
   120
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                                         130
Cys Gln Glu Pro Cys Lys Asp Thr Val Gln Ile His Asp Ile Thr Gly
                 140
                                     145
Lys Asp Cys Gln Asp Ile Ala Asn Lys Gly Ala Lys Gln Ser Gly Leu
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                                 160
Tyr Phe Ile Lys Pro Leu Lys Ala Asn Gln Gln Phe Leu Val Tyr Cys
           170
                              175
Glu Ile Asp Gly Ser Gly Asn Gly Trp Thr Val Phe Gln Lys Arg Leu
                          190
                                             195
Asp Gly Ser Val Asp Phe Lys Lys Asn Trp Ile Gln Tyr Lys Glu Gly
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                      205
                                         210
Phe Gly His Leu Ser Pro Thr Gly Thr Thr Glu Phe Trp Leu Gly Asn
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Glu Lys Ile His Leu Ile Ser Thr Gln Ser Ala Ile Pro Tyr Ala Leu
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                                 240
Arg Val Glu Leu Glu Asp Trp Asn Gly Arg Thr Ser Thr Ala Asp Tyr
                             255
                                                 260
Ala Met Phe Lys Val Gly Pro Glu Ala Asp Lys Tyr Arg Leu Thr Tyr
                          270
Ala Tyr Phe Ala Gly Gly Asp Ala Gly Asp Ala Phe Asp Gly Phe Asp
                      285
                                         290
Phe Gly Asp Asp Pro Ser Asp Lys Phe Phe Thr Ser His Asn Gly Met
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300

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 Gln Phe Ser Thr Trp Asp Asn Asp Asn Asp Lys Phe Glu Gly Asn Cys
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 Ala Glu Gln Asp Gly Ser Gly Trp Trp Met Asn Lys Cys His Ala Gly
             330
                                 335
 His Leu Asn Gly Val Tyr Tyr Gln Gly Gly Thr Tyr Ser Lys Ala Ser
                            350
 Thr Pro Asn Gly Tyr Asp Asn Gly Ile Ile Trp Ala Thr Trp Lys Thr
                        365
                                            370
 Arg Trp Tyr Ser Met Lys Lys Thr Thr Met Lys Ile Ile Pro Phe Asn
                    380
                                        385
 Arg Leu Thr Ile Gly Glu Gly Gln Gln His His Leu Gly Gly Ala Lys
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                                    400
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                               25
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Gln Cys Asp Tyr Ser Thr Gly Ser Cys Glu Pro Ile Arg Leu Gln Val
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                       55
                                           60
Pro Val Glu Ala Val Asn Met Ser Leu Gly Leu Ser Leu Ala Ala Thr
                   70
                                       75
Thr Ser Pro Pro Gln Leu Leu Ala Cys Gly Pro Thr Val His Gln Thr
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Cys Ser Glu Asn Thr Tyr Val Lys Gly Leu Cys Phe Leu Phe Gly Ser
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Asn Leu Arg Gln Gln Pro Gln Lys Phe Pro Glu Ala Leu Arg Gly Cys
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Pro Gln Glu Asp Ser Asp Ile Ala Phe Leu Ile Asp Gly Ser Gly Ser Ile Ile Pro His Asp Phe Arg Arg Met Lys Glu Phe Val Ser Thr Val Met Glu Gln Leu Lys Lys Ser Lys Thr Leu Phe Ser Leu Met Gln Tyr Ser Glu Glu Phe Arg Ile His Phe Thr Phe Lys Glu Phe Gln Asn Asn Pro Asn Pro Arg Ser Leu Val Lys Pro Ile Thr Gln Leu Leu Gly Arg Thr His Thr Ala Thr Gly Ile Arg Lys Val Val Arg Glu Leu Phe Asn Ile Thr Asn Gly Ala Arg Lys Asn Ala Phe Lys Ile Leu Val Val Ile Thr Asp Gly Glu Lys Phe Gly Asp Pro Leu Gly Tyr Glu Asp Val Ile Pro Glu Ala Asp Arg Glu Gly Val Ile Arg Tyr Val Ile Gly Val Gly Asp Ala Phe Arg Ser Glu Lys Ser Arg Gln Glu Leu Asn Thr Ile Ala Ser Lys Pro Pro Arg Asp His Val Phe Gln Val Asn Asn Phe Glu Ala Leu Lys Thr Ile Gln Asn Gln Leu Arg Glu Lys Ile Phe Ala Ile Glu Gly Thr Gln Thr Gly Ser Ser Ser Phe Glu His Glu Met Ser Gln Glu Gly Phe Ser Ala Ala Ile Thr Ser Asn Gly Pro Leu Leu Ser Thr Val Gly Ser Tyr Asp Trp Ala Gly Gly Val Phe Leu Tyr Thr Ser Lys Glu Lys Ser Thr Phe Ile Asn Met Thr Arg Val Asp Ser Asp Met Asn Asp Ala Tyr Leu Gly Tyr Ala Ala Ala Ile Ile Leu Arg Asn Arg Val Gln Ser Leu Val Leu Gly Ala Pro Arg Tyr Gln His Ile Gly Leu Val Ala Met Phe Arg Gln Asn Thr Gly Met Trp Glu Ser Asn Ala Asn Val Lys Gly Thr Gln Ile Gly Ala Tyr Phe Gly Ala Ser Leu Cys Ser Val Asp Val Asp Ser Asn Gly Ser Thr Asp Leu Val Leu Ile Gly Ala Pro His Tyr Tyr Glu Gln Thr Arg Gly Gln Val Ser Val Cys Pro Leu Pro Arg Gly Arg Ala Arg Trp Gln Cys Asp Ala Val Leu Tyr Gly Glu Gin Gly Gin Pro Trp Gly Arg Phe Gly Ala Ala Leu Thr Val Leu Gly Asp Val Asn Gly Asp Lys Leu Thr Asp Val Ala Ile Gly Ala Pro Gly Glu Glu Asp Asn Arg Gly Ala Val Tyr Leu Phe His Gly Thr Ser Gly Ser Gly Ile Ser Pro Ser His Ser Gln Arg Ile Ala Gly Ser Lys Leu Ser Pro Arg Leu Gln Tyr Phe Gly Gln Ser Leu Ser Gly Gln Asp Leu Thr Met Asp Gly Leu Val Asp Leu Thr Val Gly Ala Gln Gly His Val Leu Leu Arg Ser Gln Pro Val Leu Arg Val Lys Ala Ile Met

Glu Phe Asn Pro Arg Glu Val Ala Arg Asn Val Phe Glu Cys Asn Asp Gln Val Val Lys Gly Lys Glu Ala Gly Glu Val Arg Val Cys Leu His Val Gln Lys Ser Thr Arg Asp Arg Leu Arg Glu Gly Gln Ile Gln Ser Val Val Thr Tyr Asp Leu Ala Leu Asp Ser Gly Arg Pro His Ser Arg Ala Val Phe Asn Glu Thr Lys Asn Ser Thr Arg Arg Gln Thr Gln Val Leu Gly Leu Thr Gln Thr Cys Glu Thr Leu Lys Leu Gln Leu Pro Asn Cys Ile Glu Asp Pro Val Ser Pro Ile Val Leu Arg Leu Asn Phe Ser Leu Val Gly Thr Pro Leu Ser Ala Phe Gly Asn Leu Arg Pro Val Leu Ala Glu Asp Ala Gln Arg Leu Phe Thr Ala Leu Phe Pro Phe Glu Lys · 750 Asn Cys Gly Asn Asp Asn Ile Cys Gln Asp Asp Leu Ser Ile Thr Phe Ser Phe Met Ser Leu Asp Cys Leu Val Val Gly Gly Pro Arg Glu Phe Asn Val Thr Val Thr Val Arg Asn Asp Gly Glu Asp Ser Tyr Arg Thr Gln Val Thr Phe Phe Phe Pro Leu Asp Leu Ser Tyr Arg Lys Val Ser Thr Leu Gln Asn Gln Arg Ser Gln Arg Ser Trp Arg Leu Ala Cys Glu Ser Ala Ser Ser Thr Glu Val Ser Gly Ala Leu Lys Ser Thr Ser Cys Ser Ile Asn His Pro Ile Phe Pro Glu Asn Ser Glu Val Thr Phe Asn Ile Thr Phe Asp Val Asp Ser Lys Ala Ser Leu Gly Asn Lys Leu Leu Leu Lys Ala Asn Val Thr Ser Glu Asn Asn Met Pro Arg Thr Asn Lys Thr Glu Phe Gln Leu Glu Leu Pro Val Lys Tyr Ala Val Tyr Met Val Val Thr Ser His Gly Val Ser Thr Lys Tyr Leu Asn Phe Thr Ala Ser Glu Asn Thr Ser Arg Val Met Gln His Gln Tyr Gln Val Ser Asn Leu Gly Gln Arg Ser Pro Pro Ile Ser Leu Val Phe Leu Val Pro Val Arg Leu Asn Gln Thr Val Ile Trp Asp Arg Pro Gln Val Thr Phe Ser Glu Asn Leu Ser Ser Thr Cys His Thr Lys Glu Arg Leu Pro Ser His Ser Asp Phe Leu Ala Glu Leu Arg Lys Ala Pro Val Val Asn Cys Ser Ile Ala Val Cys Gln Arg Ile Gln Cys Asp Ile Pro Phe Phe Gly Ile Gln Glu Glu Phe Asn Ala Thr Leu Lys Gly Asn Leu Ser Phe Asp Trp Tyr Ile Lys Thr Ser His Asn His Leu Leu Ile Val Ser Thr Ala Glu Ile Leu Phe Asn Asp Ser Val Phe Thr Leu Leu Pro Gly Gln Gly Ala Phe Val Arg Ser Gln Thr Glu Thr Lys Val Glu Pro Phe Glu Val Pro Asn Pro Leu Pro Leu Ile Val Gly Ser Ser Val

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Leu Gln Val Pro Pro Glu Ala Val Asn Met Ser Leu Gly Leu Ser Leu
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Ala Ser Thr Thr Ser Pro Ser Gln Leu Leu Ala Cys Gly Pro Thr Val
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                                            90
His His Glu Cys Gly Arg Asn Met Tyr Leu Thr Gly Leu Cys Phe Leu
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                                       105
Leu Gly Pro Thr Gln Leu Thr Gln Arg Leu Pro Val Ser Arg Gln Glu
                  115
                                 120
Cys Pro Arg Gln Glu Gln Asp Ile Val Phe Leu Ile Asp Gly Ser Gly
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Ser Ile Ser Ser Arg Asn Phe Ala Thr Met Met Asn Phe Val Arg Ala
                            150
Val Ile Ser Gln Phe Gln Arg Pro Ser Thr Gln Phe Ser Leu Met Gln
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Phe Ser Asn Lys Phe Gln Thr His Leu Thr Phe Glu Glu Phe Arg Arg
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Thr Ser Asn Pro Leu Ser Leu Leu Ala Ser Val His Gln Leu Gln Gly
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                                   200
Phe Thr Tyr Thr Ala Thr Ala Ile Gln Asn Val Val His Arg Leu Phe
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                                215
His Ala Ser Tyr Gly Ala Arg Arg Asp Ala Thr Lys Ile Leu Ile Val
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Ile Thr Asp Gly Lys Lys Glu Gly Asp Thr Leu Asp Tyr Lys Asp Val
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                                           250
Ile Pro Met Ala Asp Ala Ala Gly Ile Ile Arg Tyr Ala Ile Gly Val
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Gly Leu Ala Phe Gln Asn Arg Asn Ser Trp Lys Glu Leu Asn Asp Ile
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270										280)				285
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	333	•				340	}				345	Pro	Val		gly
Ala 350	Val	. Gl3	, Sez	. Phe	355	Tr	Ser	Gly	Gly	Ala 360	Phe	Leu	Туг	Pro	Pro
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Arg	Asp	Ser	Tyx 385	Leu	Gly	Туг	Ser	Thr 390	Glu	Leu	Ala	Leu	395	Lys	Gly
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0,0					6/5		Lys			680					COF
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			705				Thr	710					716		
		, 20					Leu 725 Tyr					720			
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Asp Ser Ala Pro Val Gly Ser Gln Gly Thr Trp Ser Thr Ser Cys Arg
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Ile Asn His Leu Ile Phe Arg Gly Gly Ala Gln Ile Thr Phe Leu Ala
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Thr Phe Asp Val Ser Pro Lys Ala Val Leu Gly Asp Arg Leu Leu
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Ser Ser His Glu Gln Phe Thr Lys Tyr Leu Asn Phe Ser Glu Ser Glu
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Glu Lys Glu Ser His Val Ala Met His Arg Tyr Gln Val Asn Asn Leu
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                                 935
Gly Gln Arg Asp Leu Pro Val Ser Ile Asn Phe Trp Val Pro Val Glu
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                             950
Leu Asn Gln Glu Ala Val Trp Met Asp Val Glu Val Ser Leu Pro Gln
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Asn Pro Ser Leu Arg Cys Ser Ser Glu Lys Ile Ala Gly Pro Ala Ser
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Asp Phe Leu Ala His Ile Gln Lys Asn Pro Val Leu Asp Cys Ser Ile
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Gln Glu Ala Phe Met Arg Ala Gln Thr Thr Thr Val Leu Glu Lys
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Tyr Lys Val His Asn Pro Thr Pro Leu Ile Val Gly Ser Ser Ile
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Gly Gly Leu Leu Leu Ala Leu Ile Thr Ala Val Leu Tyr Lys
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Val Gly Phe Phe Lys Arg Gln Tyr Lys Glu Met Met Glu Glu Ala
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				415					420					425	
			430		Arg			435					440	Gly	Phe
		445			Cys		450					455			
	460				Gln	465					470			_	
475					Asn 480					485					490
				495	Leu				500					505	Leu
			510		Суз			515					520	Arg	_
		525			Gly		530					535	Phe		_
	540				Pro	545					550				
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				575	Суз				580					585	Gln
			590		Glu			595					600	Gly	
		605			Glu		610					615	•		_
	620				Ala	625					630				
635					Сув 640					645		_	_	-	650
				655	Gln				660					665	Tyr
			670		Glu			675					680	Ala	
Val	Gly	Gly 685	Thr	Val	Ala	Gly	Ile 690	Val	Leu	Ile	Gly	11e 695	Leu	Leu	Leu
	700				Leu	705					710				
715					Lys 720					725	Asn				730
Leu	Phe	Lys	Ser	Ala 735	Thr	Thr	Thr	Val	Met 740	Asn	Pro	Lys	Phe	Ala 745	Glu
Ser															

Ser